REMARKS

Claims 1-6, 8-24, and 26-37 are currently pending. Applicants note that all amendments of Claims presented herein are made without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG),[1] and without waiving the right to prosecute the amended Claims (or similar Claims) in the future.

In the office action dated 5/18/04, the Examiner made a number of rejections. The rejections are listed below in the order in which they are herein addressed.

(1) Claims 21 and 34 are rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite;

(2) Claims 1-6, 8-20, 22-24, and 26-33 are rejected under 35 U.S.C. § 103 as allegedly being obvious in light of Chong et al. (Rapid Commun. Mass Spectrometr 12:1986 [1998]); hereinafter Chong) in view of Richmond et al (Richmond et al., J. Chromatography 835:29 [1999]; hereinafter Richmond); and

(3) Claims 35-37 are rejected under 35 U.S.C. § 103 as allegedly being obvious in light of Chong taken in view of Richmond and further in view of Pandey et al. (Nature 405: 837 (2000); hereinafter Pandey).

I. The Claims are not Indefinite

The Examiner has rejected claims 21 and 34 under 35 U.S.C. 112, second paragraph, as allegedly being indefinite (Office Action, pg. 2). In particular, the Examiner states "It is unclear as what Applicants' regard as "oa"." (Office Action, pg. 2). In order to further the business interests of the Applicants and while reserving the right to prosecute the original (or similar) claims in the future, the Applicants have amended claims 21 and 34. The amended claims eliminate the abbreviation for "oa" and instead refer to electrospray ionization-orthogonal acceleration-time-of-flight mass spectrometry. As such, the applicants respectfully request that

[1] 65 Fed. Reg. 54603 (Sept. 8, 2000).

the rejection be withdrawn.

II. The Claims are not obvious

Claims 1-6, 8-24 and 26-34 stand rejected under 35 U.S.C. § 103 as allegedly being obvious in light of Chong and Richmond (Office Action, pg. 2) and Claims 35-37 as allegedly being obvious in light of Chong taken in view of Richmond and further in view of Pandey. The Applicants respectfully disagree. The Applicants submit that the examiner has failed to provide a prima facie case of obviousness. The combination of references referred to by the Examiner fails to provide a *prima facie* showing of obviousness as required by § 2143 of the Manual of Patent Examining Procedure (MPEP). There are three criteria that must be met to provide *prima facie* obviousness. The first of these criteria is a suggestion or motivation in the references or the knowledge generally available to combine the reference teachings. The second criterion is that the prior art must teach or suggest all the claim limitations. The third criteria is a reasonable expectation of success should the combination be carried out.

A. Claims 1-6, 8-24 and 26-34 are not obvious

The Applicants submit that the Examiner has failed to consider the Applicants arguments submitted in the prior response (1/2/04). As stated previously, the Applicants submit that the Examiner has failed to set forth a *prima facie* case of obviousness because none of the three criteria have been met.

In particular, the Applicants submit that the Examiner has pointed to no teaching in either Chong or Richmond to combine the references to arrive at the presently claimed invention. For example, Richmond provides no teaching that the display methods that Richmond applies to chemical samples be used in the display of protein samples, let alone multiple protein samples. The Examiner states "Richmond et al., however, states colored computer screen pictures and 3D maps provides quick and easy way of delivering liquid chromatograph (i.e. high performance liquid chromatography/HPLC data to laboratories...." (Office Action, pg. 3). The applicants submit that the above statement in fact teaches away from a combination with Chong, as evidenced by the remainder of the sentence (that the Examiner did not quote) "[t]o laboratories in traditional synthetic chemistry, combinatorial chemistry and natural products chemistry." (pg.

39, lines 19-21). This is in direct contrast to Chong and the present invention, which are directed towards analysis of **proteins** (See e.g., Claim 1).

Furthermore, as the Examiner has admitted (Office Action, pg. 3), Chong does not suggest the need for an alternate display method (*i.e.*, there is no basis in Chong or Richmond that would lead one to even contemplate modification of Chong as suggested by the Examiner).

The Applicants submit that the Examiner has instead applied improper hindsight reconstruction. Applicants submit that the case law is clear that any teaching or suggestion to combine or modify references must be found in the reference(s) themselves or in the knowledge available to one of ordinary skill in the art. They may not, as the Examiner has attempted to do, be derived from the applicant's disclosure (*In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Furthermore, the purpose of this requirement is to prevent the Examiner from using the invention itself and hindsight reconstruction to defeat the patentability of the invention (*In re Rouffet et al.*, 149 F.3d 1350, 47 USPQ2d 1453 (Fed. Cir. 1998). The Examiner is reminded, that under the law, an Examiner is not one skilled in the art and that consequently, the Examiner's opinion as to what one skilled in the art might believe is not sufficient support for a motivation to modify the teachings of the cited reference (See, *In re Rijckaert,* 9 F.3d 1531, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993)). The suggestion to combine prior art references must come from the cited references, not from the applicant's disclosure.[2] The Examiner's rejection does not establish the requisite suggestion in the art to combine elements disclosed in the prior art. "A rejection cannot be predicated on the mere identification . . . of individual components of claimed limitations. Rather, particular findings must be made as to the reasons the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed."[3] The need for a specific suggestion in the cited references is absolute: "The factual inquiry whether to combine references must be thorough and searching. It must be based on **objective evidence of record**. This precedent has been reinforced in myriad decisions and cannot be dispensed with."[4] (Emphasis added).

The Applicants further submit that even if Chong and Richmond are improperly

---

2 *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1998)

3 *Ecolochem*, 227 F.3d, 1361, 1375, 56 USPQ2d 1065, 1076, quoting *Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1317.

4 *In Re Sang Su Lee*, 277 F.3d 1338, 1341, USPQ2d 1430, 1433.

combined, they do not teach all of the elements of the presently claimed invention. In particular, neither Chong nor Richmond, alone or in combination, teach the claim element of a protein profile map that displays protein abundance and mass of a separated protein sample. In addition, neither Chong nor Richmond, even if the teachings of the two references are improperly combined, provide a teaching of a side by side display showing both protein mass and abundance of multiple samples. In rebuttal, the Examiner states "Chong et al. depict the protein profile maps side-by-side in Figure 1..." (Office Action, pg. 4). The applicants respectfully disagree. Figure 1 of Chong does not display a protein profile map "wherein said protein profile maps displays each protein as a **separate band** corresponding to said mass of said first protein sample and said second protein sample, and wherein the **intensity of said band corresponds to said protein abundance** of said first protein sample and said second protein sample." (Claim 1).

Furthermore, the Examiner has pointed to no teaching in Chong or Richmond, alone or in combination, of the elements of dependent claims 13 or 21. For example, the Examiner has pointed to no teaching (nor is any present) in Chong or Richmond of the claim element of a switchable, multichannel valve (Claims 13 and 33) or the use of Esi oa TOF mass spectroscopy (Claims 21 and 34) with the methods of the presently claimed invention. In rebuttal, the Examiner states "Chong et al. utilize the Beckman System Gold HPLC having a programmable solvent delivery module with a dual pump (switchable, multichannel valve)...." (Office Action, pg. 4). The applicants respectfully disagree and submit that the Examiner has improperly characterized "switchable, multichannel valve" and direct the Examiner to the Applicants' definition:

> "A switchable multi-channel valve allows multiple apparatus to be connected to one automated sample handler. For example, sample can first be directed through one apparatus of a system (*e.g.*, a first chromatography apparatus). The sample can then be directed through a different channel of the valve to a second apparatus (*e.g.*, a second chromatography apparatus). " Specification, pg. 14, lines 8-12.

As such, the Applicants submit that neither Chong, nor Richmond, alone or in combination, teach the claim element of a switchable, multichannel valve for use in delivering sample from one apparatus to another.

The Applicants submit that the Examiner has failed to demonstrate a prima facie case of obviousness. Nonetheless, the Applicants submit, attached to this communication, the declaration of David M. Lubman, Ph.D., an Inventor on the present application and well known

expert in the field of protein analysis. Dr. Lubman's declaration states that a scientist reading the Chong reference would have no particular motivation to alter the display methods or use different display methods, the Richmond reference would not have been consulted by someone working in the field of protein separation and analysis to solve problems in protein display, as this reference is in a different field and has no bearing on protein analysis, and there is no scientific basis in any of the references cited by the Examiner that would lead someone to apply the display methods of Richmond to the methods of Chong.

As such, the Applicants have provided evidence showing non-obviousness. The applicants respectfully request that the rejection be withdrawn.

B. Claims 35-37 are not Obvious

The Examiner has rejected Claims 35-37 35 U.S.C. § 103 as allegedly being obvious in light of Chong taken in view of Richmond and further in view of Pandey. The Examiner states "However, Chong et al. and/or Richmond et al. fail to utilize differential display to depict protein profile maps." (Office Action, pg. 5). The Examiner then cites Pandey to overcome this deficiency. The Applicants respectfully disagree and submit that Pandey does not teach this element of the claims alone or in combination with Chong and/or Richmond. The Examiner states "The process of applying differential display to mass spectrometry data is described and illustrated (page ; Figures 1 and 3). The applicants respectfully disagree and submit that Figures 1 and 3 (nor any teaching in Pandey, alone or in combination with Chong and/or Richmond) do not teach the claim element of "wherein said differential display protein profile map displays the difference in protein abundance between each protein as a **separate band** corresponding to said mass of said first protein sample and said second protein sample, and wherein the **intensity** of said band corresponds to the difference in protein abundance." (Claim 35).

Furthermore, the Examiner has pointed to no teaching in Pandey (or Chong or Richmond) to combine the teachings of the references. Indeed, the Pandey reference reviews the current state of the art in proteomics at the time the reference was published and does not point to any deficiencies in techniques used for mass spectrum display. Nor does Pandey suggest any need in the art for alternative mass spectrum display methods. The Applicants remind the Examiner of his obligation to specifically point out such teaching.

The Applicants submit that the Examiner has failed to demonstrate a prima facie case of obviousness. Nonetheless, the Applicants submit, attached to this communication, the declaration of David M. Lubman, Ph.D., an Inventor on the present application and well known expert in the art. Dr. Lubman's declaration states that a scientist reading the Pandey reference would have no particular motivation to alter the display method or use different display methods and that there is no scientific basis in any of the references cited by the Examiner that would lead someone to apply the display methods of Richmond to the methods of Pandey. As such, the Applicants have provided evidence showning non-obviousness. The applicants respectfully request that the rejection be withdrawn.

CONCLUSION

All grounds of rejection and objection of the Office Action of May 18, 2004 having been addressed, reconsideration of the application is respectfully requested. It is respectfully submitted that the Claims should be allowed. Should the Examiner have any questions, or if a telephone conference would aid in the prosecution of the present application, Applicants encourage the Examiner to call the undersigned collect at 608-218-6900.

Dated: August 18, 2004

Tanya A. Arenson
Registration No. 47,391

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105
608/218-6900